PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 09 April 2001 (09.04.01)	
International application No. PCT/GB00/02892	**Applicant's or agent's file reference** PCB/PO88452PWO
International filing date (day/month/year) 27 July 2000 (27.07.00)	**Priority date** (day/month/year) 30 July 1999 (30.07.99)
Applicant BEYNON, Robert, Jeffery et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

26 February 2001 (26.02.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer S. Mafla
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

10/031387 1645 1600

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70) 14

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PCB/JK/P088452PWO		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB00/02892	27/07/2000	30/07/1999
International Patent Classification (IPC) or national classification and IPC G01N33/68		
Applicant THE UNIVERSITY OF LIVERPOOL et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☒ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
26/02/2001	09.10.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Knudsen, H Telephone No. +49 89 2399 8696

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/02892

I. Basis f th r p rt

1. With regard to the **lem nts** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-17 as originally filed

Claims, No.:

1-11 with telefax of 03/08/2001

Drawings, sheets:

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-11
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-11
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-11
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re It m V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive st p or industrial applicability; citations and explanations supporting such statement

NOVELTY:

None of the cited prior art documents describe a method in which urinary proteins deposited on a surface are detected. Claims 1-11 are therefore considered novel.

INVENTIVE STEP:

As acknowledged in the present application's description, it is well-known in the art that rodents tend to deposit urine on all surfaces that they pass and that murine urine contain major urinary proteins (MUP) and rat urine contains α2u-globulins. It therefore appears to be obvious to the skilled person that these urinary proteins are present on surfaces on which the rodents have travelled. However, the cited prior art documents do not contain any suggestions to the skilled person that the rodents' urinary proteins could be detected on such surfaces. Claims 1-11 therefore appear to involve an inventive step.

INDUSTRIAL APPLICABILITY:

Present claims 1-11 are considered industrially applicable.

Re Item VII

Certain defects in the international application

Contrary to the requirements of Rule 5(a)(ii) PCT, the description does not identify any closest prior art document

Re Item VIII

Certain observations on the international application

8.1 The meaning of the wording "detecting for ... on a surface" in present claim 1 lacks clarity. It is not clear from the said wording that it is intended to encompass both the taking of samples from a surface, eg with a swab (see page 7, lines 3-5) and by laying a substratum on the surface and testing the substratum after it has been removed from the surface (see page 7, lines 10-14).

8.2 The only methods which have been shown to work in the description are the embodiments in which:

1) a nitrocellulose membrane is placed on a surface on which the rodents travel; and

2) a tile is placed on the surface and the urine is after removal of the tile transferred to a nitrocellulose membrane.

Thus, other embodiments which are currently claimed are not supported by the description.

The applicant is correct that it is generally not necessary to submit a working example for each and every embodiment of an invention. However, in the present case, the invention is partly based on the surprising discovery that it is possible to detect sufficient amounts of rodent proteins on natural surfaces which the animals use. It therefore appears that evidence that it is in fact possible to retrieve sufficient protein with a swab from a normal surface (ie not nitrocellulose, but carpet, wooden flooring and concrete) is necessary in order to support the invention.

CLAIMS

1. A method of detecting a rodent infestation comprising detecting for the presence of urinary proteins from rodents on a surface over which a rodent has putatively travelled and on which urinary proteins may have been deposited.

2. The method according to claim 1 wherein the urinary proteins are Major Urinary Proteins from mice.

3. The method according to claim 2 wherein the major urinary protein has an amino acid sequence as defined by Genbank Accession Numbers X00907, M16355, M16356 or X00908 and functional derivatives thereof.

4. The method according to claim 1 wherein the urinary proteins are α2u globulins from rats.

5. The method according to any preceding claim wherein the presence of urinary proteins from rodents is detected by utilising antibodies raised against the urinary protein in an immunoassay.

6. The method according to claim 5 wherein the antibodies comprise primary antibodies which binds to the urinary protein and secondary antibodies which are associated with a detectable signal and also binds to the primary antibody.

7. The method according to any preceding claim wherein swab samples are taken from the surface and the presence of urinary proteins detected on the swabs.

8. The method according to any one of claims 1-6 wherein a nitrocellulose membrane is laid on the surface and the presence of urinary proteins detected n the membrane.

9. The method according to any one of claims 1-6 wherein a substratum is laid over the surface and left for a time to allow rodents to move over, or in the vicinity of, the substratum; and the presence of urinary proteins detected on the substratum.

10. The method according to claim 9 wherein the substratum is a sheet or tile.

11. The method according to claim 9 or 10 wherein a nitrocellulose membrane is laid over the tile or sheet and the presence of urinary proteins detected on the membrane.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
PCB/P088452PWO		
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/GB 00/02892	27 July 2000	30 July 2000

Applicant

THE UNIVERSITY OF LIVERPOOL et al.

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

[x] It is also accompanied by a copy of each prior art document cited in this report.

1. [ ] Certain claims were found unsearchable (see Box I).

2. [ ] Unity of invention is lacking (see Box II).

3. [ ] The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

   [ ] filed with the international application.

   [ ] furnished by the applicant separately from the international application,

      [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

   [ ] Transcribed by this Authority

4. With regard to the title,

   [x] the text is approved as submitted by the applicant.

   [ ] the text has been established by this Authority to read as follows:

5. With regard to the abstract,

   [x] the text is approved as submitted by the applicant.

   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

   Figure No. _____

   [ ] as suggested by the applicant.

   [ ] because the applicant failed to suggest a figure.

   [ ] because this figure better characterizes the invention.

   [x] None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No:
PCT/GB 00/02892

A. CLASSIFICATION OF SUBJECT MATTER
G01N33/68,G01N33/541

According to International Patent Classification (IPC) or to both national classification and IPC[7]

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL ABSTRACTS, vol. 92, no 11, 17 March 1980 Columbus, Ohio, US; abstract no. 91729h, GROEN, A.: ' Genetically determined electrophoretic variants of the major urinary protein (Mup) complex in mouse urine' page 370; column 2; & Anim. Blood Groups Biochem. Genet., vol. 10, no. 2, 1979, pages 107-114, abstract. --	1,2
A	DATABASE WPI Week 199936	1,4,5

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search
15 September 2000

Date of mailing of the international search report
15.12.00

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentlaan 2
NL – 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer
SCHNASS

Form PCT/ISA/210 (second sheet) (July 1992)

C. (Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Derwent Publications Ltd., London, GB; Class B04, AN 1999-429835 & WO 99/27363 A1 (TANABE SEIYAKU CO) 03 June 1999 abstract. --	
A	CHEMICAL ABSTRACTS vol. 100, no. 19, 07 May 1984 Columbus, Ohio, US; abstract no. 154357s, MOTWANI, N.M.: ' Monoclonal antibodies to alpha2u-globulin and immunocytofluorometric analysis of alpha2u-globulin--synthesizing hepatocytes during androgenic induction and aging' page 346; column 2; & J. Biol. Chem., vol. 259, no. 6., 1984, pages 3653-3657, abstract. --	1,4,5
A	DATABASE WPI Week 199404 Derwent Publications Ltd., London, GB; Class B04, AN 1994-028627 & JP 05 333025 A (SUMITOMO CHEM CO LTD) 17 December 1993 abstract. --	1,4,5
A	CHEMICAL ABSTRACTS, vol. 118, no. 3, 18 January 1993 Columbus, Ohio, US; abstract no. 18214n, BOCSKEI, Z.: 'Pheromone binding to two rodent urinary proteins revealed by x-ray crystallography' page 273; column 2; & Nature, vol. 360, no. 6400, 1992, pages 186-188, abstract. ----	1,2,4

ANHANG	ANNEX	ANNEXE
Zum internationalen Recherchenbericht über die internationale Patentanmeldung Nr.	To the International Search Report to the international Patent Application No.	Au rapport de recherche international relativ à la demande de brevet international n°

PCT/GB 00/02892 SAE 293903

In diesem Anhang sind die Mitglieder der Patentfamilien der im obengenannten internationalen Recherchenbericht angeführten Patentdokumente angegeben. Diese Angaben dienen nur zur Unterrichtung und erfolgen ohne Gewähr.	This annex lists the patent family members relating to the patent documents cited in the above-mentioned search report. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.	La presénte annexe indique les membres de la famille de brevets relatifs aux documents de brevets cités dans le rapport de recherche international visée ci-dessus. Les renseignements fournis sont donnés à titre indicatif et n'engagent pas la responsibilité de l' Office.

Im Recherchenbericht angeführte Patentdokumente Patent document cited in search report Document de brevet cité dans le rapport de recherche	Datum der Veröffentlichung Publication date Date de publication	Mitglied(er) der Patentfamilie Patent family member(s) Membre(s) de la famille de brevets	Datum der Veröffentlichung Publication date Date de publication
WO A1 9927363	03-06-1999	AU A1 12603/99	15-06-1999
		JP A2 11242026	07-09-1999
JP A2 5333025	17-12-1993	none	

conversion process involves a transient interaction between HSP90 and MyoD1 and does not result in the formation of a stable tertiary complex. Conversion does not require ATP and occurs stoichiometrically in a dose-dependent fashion. HSP90 is an abundant, ubiquitous, and highly conserved protein present in most eukaryotic cells. These results provide direct evidence that HSP90 can affect the conformational structure of a DNA-binding protein.

118: 18206m **Purification and characterization of seven chloroplast ribosomal proteins: evidence that organelle ribosomal protein genes are functional and that amino-terminal processing occurs via multiple pathways in chloroplasts.** Schmidt, J.; Herfurth, E.; Subramanian, A. R. (Abt. Wittmann, Max-Planck-Inst. Mol. Genet., 33 Berlin, Germany). *Plant Mol. Biol.* 1992, 20(3), 459-65 (Eng). Putative genes for 21 ribosomal proteins (RPs) have been identified in the chloroplast DNA of four plants by nucleotide sequencing and homol. comparison but few of the gene products have been characterized. Here the purifn. and N-terminal sequencing of seven proteins from the spinach chloroplast ribosome is reported. The data show them to be the homologs of *Escherichia coli* RPs L20, L32, L33, L36, S12, S16 and S19, and thus support the view that their genes, identified in the chloroplast DNA, represent functional genes. The initiating methionine residue was not detected in the mature protein in most cases but it was present in S16, indicating that only the formyl group is removed in this case. This result and the previously reported finding of N-Me alanine at the N-terminus of chloroplast L2 indicate the existence of multiple N-terminal processing pathways in the chloroplast.

118: 18207n **Sequencing of the primary adhesion domain of bovine von Willebrand factor.** Bakhshi, Meenakshi R.; Myers, Jeanne C.; Howard, Pamala S.; Soprano, Dianne R.; Kirby, Edward P. (Sch. Med., Temple Univ., Philadelphia, PA 19140 USA). *Biochim. Biophys. Acta* 1992, 1132(3), 325-8 (Eng). A cDNA library, constructed from bovine heart endothelial cell poly(A)+ RNA, was screened using a *Bst*XI fragment of human von Willebrand factor (vWF) cDNA as a probe. This probe codes for the major adhesion domain of vWF that includes the GPIb, collagen and heparin binding domains. Of the ten pos. clones obtained, a clone that spanned the region of interest was sequenced by the dideoxynucleotide method yielding a sequence of 1550 bp. This region of the bovine cDNA codes for amino acids corresponding to #262 to #777 in human vWF and encompasses the entire pro adhesion domain. Both the nucleotide sequence and the deduced amino acid sequence are 82% homologous to those of human vWF. Cysteine residues #471, 474, 509 and 695, which form intrachain bonds in human vWF, are also present in the bovine vWF sequence.

118: 18208p **Systematic mutational analysis of the yeast ACT1 gene.** Wertman, Kenneth F.; Drubin, David G.; Botstein, David (Genentech, Inc., South San Francisco, CA 94080 USA). *Genetics* 1992, 132(2), 337-50 (Eng). The isolation and characterization of a synoptic set of site-directed mutations distributed throughout the single actin gene of *Saccharomyces cerevisiae* is reported. Mutations were systematically targeted to the surface of the protein by identifying clusters of 2 or more charged residues in the primary sequence; every charged residue in a cluster was replaced with alanine. Mutations were recovered in high yield (34 of 36 constructed) as heterozygous diploids. Mutant phenotypes were examd. in haploid segregants: 11 were recessive lethal, 16 conditional-lethal (including temp.-sensitive and salt-sensitive) and 7 had no discernible phenotype. Genetic anal. suggested that the two mutations constructed but not recovered in yeast may have a dominant defective phenotype. Location of the mutant residues on the three-dimensional structure of the rabbit muscle actin monomer confirmed that most (81%) of the charged residues altered lie at or near the surface of the protein, confirming a key assumption of the method. Many of the new *act1* alleles have properties readily interpreted in light of the actin structure and should prove useful in both genetic and biochem. studies of actin function.

118: 18209q **The ANK repeat: a ubiquitous motif involved in macromolecular recognition.** Michaely, Peter; Bennett, Vann (Med. Cent., Duke Univ., Durham, NC 27710 USA). *Trends Cell Biol.* 1992, 2(5), 127-9 (Eng). Many proteins rely on stable, noncovalent interactions with other macromols. to perform their function. The identification of a repeated sequence motif, the ANK repeat, in diverse proteins whose common function involves binding to other proteins indicates one way nature may achieve a wide range of protein-protein interactions. In this article, evidence is described that these ANK repeats are involved in the specific recognition of proteins and possibly DNA, and present a model for the folding of the motif.

118: 18210h **Molecular shape of dystrophin.** Sato, Osamu; Nonomura, Yoshiaki; Kimura, Sumiko; Maruyama, Koscak (Fac. Sci., Chiba Univ., Chiba, Japan 263). *J. Biochem. (Tokyo)* 1992, 112(5), 631-6 (Eng). The mol. shape of dystrophin has been reported to be a 175 nm flexible rod or a 120 nm dumbbell. The present work revealed that 100 nm flexible rods with or without spheres were predominant in highly purified dystrophin prepns. When the sample was subjected to gel filtration, dystrophin oligomers were isolated just after the void vol. and the fraction largely consisted of dumbbell-shaped mols. From various rotary-shadowed images, it was suggested that dystrophin is a rod with spheres at both ends, approx. 110 nm long and 2 nm wide. It appeared that this monomer binds to another monomer in a staggered way, forming a dimer, and the dimers assoc. with each other side-by-side, forming a dumbbell-shaped tetramer, 130 nm long and 5 nm wide. The tetramers form an end-to-end aggregate. It seemed that the dumbbell structure was not affected by alk. (pH 11) treatment to dissoc. dystrophin assocd. glycoproteins, but was deteriorated by detergents (NP-40, Triton X-100, or CHAPS) used for solubilization of membrane-bound dystrophin.

118: 18211j **Structure of a fibronectin type III domain from tenascin phased by MAD analysis of the selenomethionyl protein.** Leahy, Daniel J.; Hendrickson, Wayne A.; Aukhil, Ikramuddin; Erickson, Harold P. (Dep. Biochem. Mol. Biophys., Columbia Univ., New York, NY 10032 USA). *Science (Washington, D. C., 1883-)* 1992, 258(5084), 987-91 (Eng). Fibronectin type III domains are found in many different proteins including cell surface receptors and cell adhesion mols. The crystal structure of one such domain from the extracellular matrix protein tenascin was detd. The structure was solved by multiwavelength anomalous diffraction (MAD) phasing of the selenomethionyl protein and has been refined to 1.8 angstrom resoln. The folding topol. of this domain is identical to that of the extracellular domains of the human growth hormone receptor, the second domain of CD4, and PapD. Although distinct, this topol. is similar to that of Ig const. domains. An Arg-Gly-Asp (RGD) sequence that can function for cell adhesion is found in a tight turn on an exposed loop.

118: 18212k **The critical role of asparagine 502 in post-translational alteration of protein 4.1.** Inaba, Mutsumi; Maede, Yoshimitsu (Fac. Vet. Med., Hokkaido Univ., Sapporo, Japan 060). *Comp. Biochem. Physiol., B: Comp. Biochem.* 1992, 103B(3), 523-6 (Eng). Band 4.1 protein in most mammalian erythrocytes exhibits a post-translational conversion of 4.1b to 4.1a, except for feline protein 4.1, which lacks this alteration. A previous study provided evidence that protein 4.1b in human erythrocytes is converted to 4.1a by deamidation of Asn-502, suggesting that the post-translational change of 4.1b to 4.1a depends on the primary structure of the protein at the site of deamidation. To confirm this hypothesis, proteolytic fragments corresponding to the deamidation site of human protein 4.1 were purified from canine and feline erythrocyte protein 4.1 and analyzed for their amino acid sequences. Two proteolytic peptides, D7 and D9 derived from canine protein 4.1, both corresponding to the human sequence Thr-492-...-Asn(or Asp)-502-...-Lys-505 showed the same sequence, Thr-Gln-Thr-...-Lys, except that the 11th residue equiv. to the 502nd amino acid was Asn in D7 whereas it was Asp in D9, indicating that deamidation occurs at the same position in canine protein 4.1 as in humans. However, substitution of Ser for Asn at this position was obsd. in feline protein 4.1. These results demonstrated that Asn-502 plays a crit. role in post-translational conversion of 4.1b to 4.1a in mammalian erythrocytes.

118: 18213m **Ring finger in the peroxisome assembly factor-1.** Patarca, Roberto; Fletcher, Mary Ann (Sch. Med., Univ. Miami, Miami, FL 33138 USA). *FEBS Lett.* 1992, 312(1), 1-2 (Eng). Peroxisome assembly factor 1 (PAF-1) is reported here to contain the signature subsequence for a ring finger motif in its C-terminal region. This conserved subsequence in PAF-1 may be the key to a gene expression regulatory pathway important in peroxisome biogenesis.

118: 18214n **Pheromone binding to two rodent urinary proteins revealed by x-ray crystallography.** Bocskei, Zsoit; Groom, Colin R.; Flower, Darren R.; Wright, Charles E.; Phillips, Simon E. V.; Cavaggioni, Andrea; Findlay, John B. C.; North, Anthony C. T. (Dep. Biochem. Mol. Biol., Univ. Leeds, Leeds, UK LS2 9JT). *Nature (London)* 1992, 360(6400), 186-8 (Eng). The three-dimensional structures of mouse major urinary protein (at 2.4 Å resoln.) and rat urinary α2-globulin (at 2.8 Å resoln.) are reported here. The results corroborate the role of these proteins in pheromone transport and elaborate the structural basis of ligand binding.

118: 18215p **Identification and molecular analysis of a 63-kilodalton stress protein from Neisseria gonorrhoeae.** Pannekoek, Yvonne; Van Putten, Jos P. M.; Dankert, Jacob (Dep. Med. Microbiol., Univ. Amsterdam, 1105 AZ Amsterdam, Neth.). *J. Bacteriol.* 1992, 174(21), 6928-37 (Eng). Iron limitation, glucose deprivation, and growth under low oxygen supply (environmental stress) increased the expression of several proteins of *Neisseria gonorrhoeae*, including a 63-kilodalton protein identified by SDS-PAGE. This gonococcal stress protein (GSP63) was detected in the cytosol and copurified with lithium acetate-derived outer membranes. Successful purifn. of the protein was achieved by sucrose d. gradient centrifugation and by chromatog. on phenyl-Sepharose. Gel filtration of the purified protein revealed a mol. wt. of approx. 450,000, suggesting that in its native state, the protein consists of a multimer of 6-8 subunits. Isoelec. focusing indicated a pI of 5.2. Immunoblotting expts. using a polyclonal antiserum raised against the purified protein demonstrated cross-reactivity with a protein of the same electrophoretic mobility as GSP63 in all 8 gonococcal isolates tested. N-terminal amino acid sequencing of the protein revealed up to 65% homol. with members of the Hsp60 heat shock protein family, suggesting that GSP63 is related to this group of proteins. This relationship was further substantiated by the immunol. cross-reactivity of GSP63 with mycobacterial Hsp60 and the ATP-binding activity of the gonococcal stress protein.

118: 18216q **Chemical-shift ranges in proteins.** Augspurger, Joseph; Pearson, John G.; Oldfield, Eric; Dykstra, Clifford E.; Park, Ki Deok; Schwartz, Dwight (Dep. Chem., Indiana Univ. Purdue Univ., Indianapolis, IN 46205 USA). *J. Magn. Reson.* 1992, 100(2), 342-57 (Eng). The results of ab initio deriv. Hartree-Fock calcns. of the dipole and quadrupole shielding polarizabilities and hyperpolarizabilities of a no. of small mols. are reported, together with esta. of the elec. fields and field gradients present in proteins. It is argued that weak elec. interactions, mediated via these shielding polarizabilities, make major contributions to the chem.-shift nonequivalencies obsd. in proteins due to folding into their native

CHEMICAL ABSTRACTS®

V 1. 118 JANUARY 18, 1993 N . 3

1—PHARMACOLOGY

C. PAUL BIANCHI

This section includes the biochemical, physiological, and toxic effects of drugs or potential drugs, their metabolism, analysis in biological systems, and structure–activity relations. Gene therapy is included, but drug genetic engineering methodology is included in Section 3; commercial production of drugs by genetically engineered organisms or cells is included in Section 16. Drug formulations are included in Section 63; analysis of drug formulations appears in Section 64; the pharmacology of hormones and agents affecting reproduction, e.g., contraceptives, in Section 2; radiopharmaceuticals, in Section 8; effects of antibiotics, bactericides, etc., on microorganisms in vitro are placed in Section 10; studies emphasizing the synthesis of drugs are placed in the appropriate synthetic organic or inorganic section; drugs used only as tools appear in the section appropriate to the organism or process under study.

118: 15680a **Phototoxic and photoallergic reactions.** Schauder, Silvia (Hautklin., Univ. Goettingen, W–3400 Goettingen, Germany). *Dtsch. Apoth. Ztg.* **1992**, 132(21), 1123–8 (Ger). A review, with 16 refs., describing exogenic photosensitizers which elicit phototoxic or photoallergic reactions in humans either via direct skin contact (e.g. topical drug forms, sunscreens, cosmetics) or following transportation via the blood to the skin (e.g. other drug forms, food components, occupational chems.).

118: 15681b **Antioxidants and their action mechanism.** Inoue, Masayasu; Kunitomo, Ryuji (Kumamoto Univ., Kumamoto, Japan). *Chiryogaku* **1992**, 26(5), 573–80 (Japan). A review with 16 refs. on the potential and problems of the application of antioxidants in medicine. The antioxidants discussed include: natural antioxidants, thiol compds., vitamin C, and lipophilic antioxidants (esp. vitamin E).

118: 15682c **Plant antioxidants as anticarcinogens.** Osawa, Toshihiko (Dep. Food Sci. Technol., Nayoga Univ., Chikusa, Japan 464–01). *Anticarcinog. Radiat. Prot. 2, [Proc. Int. Conf.], 3rd* 1989 (Pub. 1991), 327–36 (Eng). Edited by Nygaard, Oddvar F.; Upton, Arthur C. Plenum: New York, N. Y. A review with 30 refs.

118: 15683d **Purines and pyrimidines in malarial parasites. Commentary.** Van Dyke, Knox (Sch. Med., West Virginia Univ., Morgantown, WV 26506 USA). *Blood Cells* **1990**, 16(2–3), 485–95 (Eng). A commentary and review with 28 refs.

118: 15684e **Glucobay (acarbose).** Sturm, M. (Abt. Forsch. Entwickl., Bayer Austria G.m.b.H., A–1011 Vienna, Austria). *Wien. Klin. Wochenschr.* **1992**, 104(11), 329–36 (Ger). A review, with 51 refs., of the pharmacol. of the title α–glucosidase inhibitor and antihyperglycemic.

118: 15685f **Hivid (2',3'–dideoxycytidine; ddC).** Toeglhofer, W. (Hoffmann–La Roche Wien G.m.b.H., A–1030 Vienna, Austria). *Wien. Klin. Wochenschr.* **1992**, 104(12), 363–7 (Ger). A review, with 13 refs., summarizing the pharmacol. of the 2'–deoxycytidine analog ddC, a HIV–1 and –2 reverse transcriptase inhibitor.

118: 15686g **Ergoline derivatives. "Dirty", specific, and selective drugs.** Eich, Eckart (Inst. Pharm. Biol., Freie Univ. Berlin, W–1000 Berlin, 33 Germany). *Pharm. Ztg.* **1992**, 137(22), 9–16, 18–20, 22 (Ger). A review, with 51 refs. describing the pharmacol. of the ergot alkaloids and related compds. as the basis for their current and potential clin. application.

118: 15687h **Clarithromycin – a new macrolide antibiotic.** Schulz, Juergen (Arzneimittelinformationsstelle, Bundesver. Dtsch. Apothekerverb., W–6000 Frankfurt/Main, 1 Germany). *Pharm. Ztg.* **1992**, 137(22), 34–5, 38–9 (Ger). A review, with 16 refs., of the pharmacol. of the title erythromycin deriv.

118: 15688j **Transporters of delight.** Sabol, Karen E.; Seiden, Lewis S. (Dep. Pharmacol. Physiol., Univ. Chicago, Chicago, IL 60637 USA). *Curr. Biol.* **1992**, 2(8), 414–16 (Eng). A review, with 25 refs., on the effects of amphetamine and methylenedioxymeth= amphetamine on the release of dopamine and serotonin from intracellular vesicular storage pools.

118: 15689k **Is there a specific therapy of liver fibrosis?** Hoegemann, B. (Med. Klin. Poliklin. B, Westfael. Wilhelms–Univ., W–4400 Muenster, Germany). *Z. Gastroenterol.* **1992**, 30(5), 333–6 (Ger). A review, with 64 refs., which describes the mode of action of drugs which interfere at particular levels of collagen metab. and which may thus prove effective for the treatment of chronic liver diseases assocd. with fibrotic transformation.

118: 15690d **Use of CCK–antagonists for physiological or therapeutical studies.** Heintges, T.; Niederau, C. (Med. Klin. Poliklin., Heinrich–Heine–Univ., W–4000 Duesseldorf, 1 Germany). *Z. Gastroenterol.* **1992**, 30(5), 337–43 (Ger). A review, with 70 refs., outlining the potential of cholecystokinin (CCK) receptor antagonists for investigating the physiol. role of CCK and, as a consequence, for the treatment of digestive tract and pancreatic disorders.

118: 15691e **Hypnotics and anxiolytic drugs.** Ohtsubo, Tempei; Kamijima, Kunitoshi (Sch. Med., Showa Univ., Tokyo, Japan 142). *J. Jpn. Soc. Hosp. Pharm.* **1992**, 28(7/8), 773–9 (Japan). A review with 8 refs., on the clin. use of hypnotics and antianxiety drugs. The side effects and the use of benzodiazepine for elderly patients were described. K. Yoshikawa

118: 15692f **Drug side effects on the skin.** Bork, Konrad (Hautklin., Johannes–Gutenberg–Univ., W–6500 Mainz, Germany). *Med. Klin. (Munich)* **1992**, 87(6), 329–33 (Ger). A review, with 26 refs., describing the various types of skin reactions to drugs and their causes and frequency, new types of skin side effects, and diagnostic methods.

118: 15693g **Amiodarone and disturbances of the thyroid function – pathogenesis, diagnosis, treatment.** Gasinska, Teresa (I Klin. Chorob Wewn., Slaska Akad. Med., 40–029 Katowice, Pol.). *Pol. Tyg. Lek.* **1991**, 46(43–44), 841–3 (Pol). A review with 44 refs. discussing the effect of amiodarone on metab. of thyroid hormones and immunol. processes in the thyroid as well as noxious sequelae of the amiodarone therapy. J. Geisler

118: 15694h **Effect of adrenergic blockers on lipids and their derivatives.** Ilczyszyn, Wieslaw; Tuszynski, Henryk (II Oddzial Chorob Wewn., Szpital Marynarki Wojen., Gdansk–Oliwa, Pol.). *Lek. Wojsk.* **1991**, 67(5–6), 363–5 (Pol). A review, with 24 refs. J. Geisler

118: 15695j **Taxol: a review of its preclinical in vivo antitumor activity.** Rose, William C. (Exp. Ther. Dep., Bristol–Myers Squibb Co., Wallingford, CT 06492 USA). *Anti–Cancer Drugs* **1992**, 3(4), 311–21 (Eng). A review with 22 refs. Taxol has been demonstrated in numerous labs. worldwide to have broad–spectrum antitumor activity against many tumor models. The susceptible tumors include murine leukemias and solid tumors, and human solid tumor xenografts. The initial findings of taxol's ineffectiveness against most distal site tumor models was probably a consequence of the insoly. of taxol in nearly all the vehicles used in those early studies. On the occasions when an ethanol–based vehicle was used to dissolve taxol, substantial distal site antitumor activity was obsd. Although no definitive schedule dependency data have evolved, once–a–day or every–other–day i.v. injections for several treatments have proved to be reproducibly effective in stringent s.c. tumor models. Attempts to discern a therapeutically synergistic cytotoxic drug combination was made on two occasions without success. In the manner evaluated, taxol plus either adriamycin, cisplatin, cyclophosphamide or etoposide (VP–16) were not meaningfully more efficacious than the more effective drug in each of those combination settings.

118: 15696k **DNA toposiomerase–targeting antitumor agents and drug resistance.** Takano, Hiroshi; Kohno, Kimitoshi; Matsuo, Kenichi; Matsuda, Takao; Kuwano, Michihiko (Dep. Biochem., Oita Med. Univ., Oita, Japan 879–55). *Anti–Cancer Drugs* **1992**, 3(4), 323–30 (Eng). A review with 63 refs. of the chemotherapeutic agents which have been developed by targeting DNA topoisomerase I and II. Camptothecins as topoisomerase I–targeting agents and newly developed topoisomerase II–targeting agents with unique properties are expected to be promising anticancer agents in the near future. An important issue is how cellular sensitivity to these agents is controlled. One approach is to establish and characterize drug–resistant human cancer cell lines, which would provide powerful tools to understand their intracellular target sites and also the mechanisms for acquisition of drug resitance to topoisomerase inhibitors. Drug resistance to topoisomerase–targeting agents appears to be closely correlated with two events, namely decreased expression and point mutation of topoisomerase genes.

118: 15697m **Inhibition of metastasis of mouse B16 melanoma by βm actin.** Sadano, Hiroyuki; Taniguchi, Shunichiro (Med. Inst. Bioregul., Kyushu Univ., Fukuoka, Japan 812). *Jikken Igaku* **1992**, 10(17), 2308–15 (Japan). A review with 20 refs. on the title subject. K. Yoshikawa

118: 15698n **Chemotherapy in the elderly.** Furue, Hisashi (Sch. Med., Teikyo Univ., Tokyo, Japan). *Gan to Kagaku Ryoho* **1992**, 19(11), 1796–800 (Japan). A review with 17 refs. Because of the increase in the incidence of malignancies with advancing age, the adequate chemotherapy of elderly patients with cancer is required. In leukemia and Hodgkin's lymphoma, definite trends of decreased levels of response and survival in relationship to increased age have been reported. This reduced rates of response in elderly leukemia

AN - 1999-429835 [36]
AP - WO1998JP05319 19981126; AU19990012603 19981126; [Based on WO9927363]
; JP19980331828 19981124
PR - JP19970323684 19971126
TI - Examining kidney diseases by detecting fatty acid binding protein
IW - KIDNEY DISEASE DETECT FATTY ACID BIND PROTEIN
IN - HONDA A; KIMURA K; SUGAYA T; UCHIDA H; YAMANOUCHI M
PA - (TANA) TANABE SEIYAKU CO
PN - WO9927363 A1 19990603 DW199936 G01N33/53 Jpn 031pp
- AU1260399 A 19990615 DW199944 G01N33/53 000pp
- JP11242026 A 19990907 DW199947 G01N33/50 011pp
ORD - 1999-06-03
IC - G01N33/50 ; G01N33/53 ; G01N33/68
FS - CPI
DC - B04
DS - BE CY EA FR GR IE IT MC NL OA SZ
DN - AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE
GH GM HR HU ID IL IS KE KG KR KZ LC LK LR LS LT LU LV MD MG MK MN MW
MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AB - WO9927363 NOVELTY - Kidney diseases are examined by detecting a fatty acid-binding protein derived from kidney tissues in a specimen collected from mammals other than rodents.
- DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
- (1) examining kidney diseases of rodents except alpha 2U-globulin nephropathy by detecting alpha 2U-globulin or a fatty acid-binding protein derived from the kidney tissues in specimens obtained from rodents such as rats and mice and comparing the results with those produced with normal tissues and
- (2) a diagnostic reagent or kit for use in the examination of kidney diseases.
- ACTIVITY - None given.
- MECHANISM OF ACTION - None given.
- USE - The method is used to examine kidney diseases in mammals except rodents, to provide test results applicable in diagnosis of the prognosis of the diseases and as a basis for selection of appropriate therapy with consideration of risks concerning the prognosis.
- ADVANTAGE - The method is simple and efficient and is applicable to kidney tissues and urine.

92: 91721z **Genetic variants of hemoglobin in canine erythrocytes.** Tanabe, Yuichi; Omi, Tokiyoshi; Ota, Katuaki (Fac. Agric., Gifu Univ., Gifu, Japan 504). *Anim. Blood Groups Biochem. Genet.* 1978, 9(2), 79–83 (Eng). Genetic polymorphism of Hb was found in the erythrocytes of dogs of 7 Japanese native breeds with starch-gel electrophoresis. Anal. of parentage records of the dogs revealed that the phenotypic variation of Hb was controlled by 1 autosomal locus with 2 codominant alleles, Hb^A and Hb^B. The allele Hb^A occurred only in Japanese native breeds except Shikoku. The frequency of Hb^A in the Japanese breeds was 0.08. All the dogs belonging to 25 European breeds and 5 oriental origin (except Japan) breeds examd. in this expt. had the homozygous genotype constitution Hb^B/Hb^B.

92: 91722a **Polymorphism of ^{14}C-vitamin D_3 binding protein in cattle and water buffalo serum.** Masina, P.; Ramunno, L.; Iannelli, D. (Inst. Anim. Prod., Univ. Naples, 80055 Portici, Italy). *Anim. Blood Groups Biochem. Genet.* 1978, 9(3), 133–7 (Eng). The polymorphism of vitamin D_3-binding protein was studied in cattle and water buffalo serum. In cattle, 3 phenotypes were obsd. (A, AB, and B). The 3 phenotypes were controlled by 2 autosomal codominant alleles. The frequencies of the *A* and *B* alleles were 0.255 and 0.745, resp. The distribution of the phenotypes was consistent with the Hardy–Weinberg law. In the water buffalo, 6 phenotypes were obsd. (A, B, C, AB, AC, and BC). The phenotypes were detd. by 3 autosomal codominant alleles (A, B, and C). The frequencies of the A, B, and C alleles were 0.414, 0.440, and 0.146, resp. This phenotype distribution was also consistent with the Hardy–Weinberg law.

92: 91723b **The hemopexin locus: its assignment to linkage group I in the laboratory rabbit (Oryctolagus cuniculus) and evidence for a fourth allele.** Hagen, K. L.; Suzuki, Y.; Tissot, R.; Cohen, C. (Med. Cent., Univ. Illinois, Chicago, IL 60612 USA). *Anim. Blood Groups Biochem. Genet.* 1978, 9(3), 151–9 (Eng). The hemopexin locus phenotypes were detd. for rabbits with polyacrylamide gel electrophoresis, and the presence of a 4th allele at this locus was revealed. Of the 19 mating types segregating at this locus, 17 demonstrated segregation ratios consistent with the hypothesis of a 4-allele, codominant, autosomal system. Studies of 3 of the largest inbreeding lines indicated that fixation at this locus has occurred in 2 of them. Linkage studies showed that the *Hx* locus is located between the color locus, *c*, and the *Hq* blood group locus; therefore it is assigned to Linkage Group I of the rabbit.

92: 91724c **NADH diaphorase as a genetic marker for sheep red cells.** Tucker, E. M.; Crowley, C. (Inst. Anim. Physiol., ARC, Babraham/Cambridge, Engl. CB2 4AT). *Anim. Blood Groups Biochem. Genet.* 1978, 9(3), 161–7 (Eng). Three NADH diaphorase phenotypes were obsd. in the red cells of sheep. Breeding data indicated that this polymorphism was under the control of 2 autosomal codominant alleles, designated Dia^F and Dia^S. Phenotype Dia F had significantly lower NADH diaphorase activity than did phenotype Dia S. The frequency of Dia^F and Dia^S was detd. in 9 different breeds.

92: 91725d **Studies on serum albumin in Korean cattle.** Suzuki, Shozo; Han, Sang Kee (Inst. Anim. Serol., Tokyo Univ. Agric., Tokyo, Japan). *Anim. Blood Groups Biochem. Genet.* 1978, 9(3), 181–2 (Eng). The serum albumin types from native Korean cattle were studied. All but 1 of the samples was classified as phenotype Alb AA or Alb AB. One sample exhibited the A zone in conjunction with a new zone which migrated to a position just blow that of the B zone. The zone was designated as Alb I Korea and the phenotype as AI. In the absence of ref. samples it was not possible to det. whether Alb I Korea identifies with 1 or another of those zones. The Alb^A, Alb^B, and Alb^I alleles had gene frequencies of 0.989, 0.010, and 0.001, resp.

92: 91726e **Studies on adenosine deaminase (ADA) polymorphism in Danish cattle.** Larsen, B.; Hyldgaard-Jensen, J.; Aagaard, Lise (Dep. Physiol. Endocrinol. Bloodgrouping, R. Vet. Agric. Univ., Copenhagen, Den.). *Anim. Blood Groups Biochem. Genet.* 1978, 9(3), 191–3 (Eng). All 10 previously described ADA phenotypes were obsd. in leukocytes of Danish cattle breeds, and the phenotypes obsd. in dam-offspring pairs were in agreement with control by 4 codominant alleles. The gene frequencies in 3 Danish cattle breeds were detd. Among the 4 genes (ADA^A–ADA^D), ADA^A had a low frequency in 2 of the breeds, and ADA^C had a frequency of ~0.5 in the 3 breeds. Based on the gene frequencies, the probability of excluding a falsely accused sire or dam (both parents tested) by the ADA system was estd. as 37.8% in Red Danish, 42.0% in White Danish, and 30.7% in Jersey cattle, the max. effect of a 4 allele codominant system being 50.4%. Among 14 blood group or protein loci tested, close to moderate linkage between the ADA system and 13 of the loci was excluded. For the remaining F blood group system, the available material was insufficient for any conclusion, but the lod score (likelihood ratio) was pos. For the L and S blood group systems, the max. lod scores were pos., but the accumulated scores were neg.

92: 91727f **Isoelectric focusing of horse serum esterase isozymes and detection of new phenotypes.** Fisher, R. A.; Scott, A. M. (Galton Lab., Univ. Coll. London, London, Engl. NW1 2HE). *Anim. Blood Groups Biochem. Genet.* 1978, 9(4), 207–13 (Eng). Isoelec. focusing in flat bed acrylamide gels was used to sep. serum esterase isoenzymes from *Equus caballus* (both horses and ponies) and *Equus przewalskii*, and new phenotypes were detected among the breeds examd. The resoln. with isoelec. focusing was better than that with starch gel electrophoresis. The active products of 6 different alleles previously identified (Es^F, Es^G, Es^P, Es^H, Es^I, and Es^X, where Es^P is for the Przewalskii horse only) were found, and 3 isoenzyme patterns (F_1, R, and L) presumably under the control of another 3 alleles (Es^{F1}, Es^R, and Es^L) were identified. Two apparently silane alleles (with inactive products) were detected, P^o from Przewalskii horses and I^o from Mongolian ponies.

92: 91728g **Further studies on bovine serum amylase – the effect of gel buffer pH.** Archibald, A. L.; Spooner, R. L. (Anim. Breed. Res. Organ., ARC, Edinburgh, Scot. EH9 3JQ). *Anim. Blood Groups Biochem. Genet.* 1978, 9(4), 229–38 (Eng). The effect of electrophoresis gel buffer pH on the resoln. of bovine serum amylase (amylase I) isoenzymes was studied and the consequences for understanding the genetics of this locus are discussed. The optimal sepn. of amylase isoenzymes was achieved with a gel buffer of pH 8 with which 5 different isoenzymes were resolved. Isoenzyme E, a satellite to isoenzyme C, had the same mobility as the B isoenzyme at pH 7.3 but migrated slower than B at pH 8.0. The D isoenzyme was only obsd. in samples contg. A or B activity and is thus considered to be a secondary isoenzyme of A or B. The obsd. and expected nos. of amylase I types in offspring from different matings in British cattle are presented; of 23 mating classes, 22 supported the hypothesis of a monogenic inheritance of the *AmI* locus controlled by 3 codominant alleles (*AmI A*, *AmI B*, *AmI C*). Some of the differences reported in the literature for *AmI* gene frequencies and allele nos. may be the result of different electrophoretic techniques used rather than population differences.

92: 91729h **Genetically determined electrophoretic variants of the major urinary protein (Mup) complex in mouse urine.** Groen, A.; Lagerwerf, A. J. (Fac. Vet. Med., Univ. Utrecht, Neth.). *Anim. Blood Groups Biochem. Genet.* 1979, 10(2), 107–14 (Eng). The Mup-complex excreted in mouse urine was studied electrophoretically both on starch gel and on cellogel (cellulose acetate). On starch gel, 6 anodally migrating protein bands were obsd. These bands were designated component 3, 2', 2, 1, and 4 (i.e., 2 bands) in the order of decreasing mobility toward the anode. The slower protein band of component 4 on starch gel was not obsd. on cellogel. By testing mouse inbred strains, 5 male and 4 female Mup phenotypes were distinguished. Test crosses suggested a 4-allelic (*a*, *b*, *c*, *d*) variation with regard to components 2', 2, and 1: group A strains showed component 1, group B strains components 1 and 2, group C and group F strains none, and group D strains showed components 1 and 2'. Component 3 may be encoded by another Mup locus, although no crossing-over was obsd.: presence of this component (A, B, D, and F strains), absence (C strains). Insufficiently reproducible demonstration of the variation with regard to component 4 forced the exclusion of this component for strain distinction. The Mup phenotypes described can be useful for the detection of certain strain contaminations, esp. if F_1 hybrid Mup phenotypes are distinguishable.

92: 91730b **An unusual transferrin variant in sheep.** Glasnak, V.; Stratil, A. (Anim. Breed. Res. Inst., 252 09 Hradistko, Czech.). *Anim. Blood Groups Biochem. Genet.* 1979, 10(2), 115–20 (Eng). An unusual variant, transferrin (Tf) Aw, was found in sheep transferrins. Its position in starch gel electrophoresis was identical with that of the variant Tf A, but the intensity of corresponding bands was substantially lower. Family analyses proved that the variant Aw is genetically controlled and represents either the product of an unusual allele *Tf Aw* or the interaction between the allele *Tf A* and a hypothetical modifying locus.

92: 91731c **Genetic polymorphism of eserine resistant esterases in canine plasma.** Sugiura, Shuji; Tanabe, Yuichi; Ota, Katuaki (Fac. Agric., Gifu Univ., Gifu, Japan 504). *Anim. Blood Groups Biochem. Genet.* 1977, 8(3), 121–6 (Eng). The genetic polymorphism of plasma eserine-resistant esterases was studied in European, Chinese, and Japanese dog breeds. After electrophoresis 9–10 bands of nonspecific esterases were found in canine plasma. Six phenotypic variants were obsd. The 6 esterase variants are controlled by 1 autosomal locus (*Es*) with 3 codominant alleles (Es^A, Es^B, and Es^C). The gene frequency of Es^B was the highest in most of the breeds examd. The Es^C allele occurred only in 5 Japanese native breeds (Akita, Shikoku, Hokkaido, Shinshi-Shiba, and Mino-Shiba) and in 1 Spitz dog. Its frequency was relatively high in the Akita (0.25) and Shikoku (0.30) breeds.

92: 91732d **Polymorphism of 6-phosphogluconate dehydrogenase in the leukocytes of cattle.** Probeck, H. D.; Geldermann, H. (Tieraerztl. Inst., Univ. Goettingen, Goettingen,

CHEMICAL ABSTRACTS®

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1—PHARMACODYNAMICS

Available in the computer-readable file *Chemical-Biological Activities (CBAC)*

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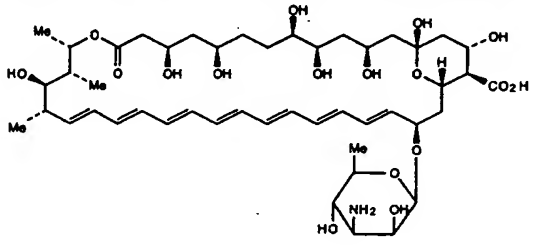
92: 87639m **Platinate toxicity: past, present, and prospects.** Guarino, A. M.; Miller, D. S.; Arnold, S. T.; Pritchard, J. B.; Davis, R. D.; Urbanek, M. A.; Miller, T. J.; Litterst, C. L. (Lab. Toxicol., Natl. Cancer Inst., Bethesda, MD USA). *Cancer Treat. Rep.* 1979, 63(9–10), 1475–83 (Eng). A review with 22 refs.

92: 87640e **Nucleoside 3',5'-cyclic monophosphate metabolites of purine analogs. Possible role as physiological mediators.** Zimmerman, Thomas P. (Dep. Exp. Ther., Wellcome Res. Lab., Research Triangle Park, NC 27709 USA). *Biochem. Pharmacol.* 1979, 28(17), 2533–9 (Eng). A review with 120 refs.

92: 87641f **Towards selectivity in cancer chemotherapy: a biochemical overview.** Harrap, K. R. (Dep. Biochem. Pharmacol., Inst. Cancer Res., Sutton/Surrey, Engl.). *Adv. Enzyme Regul.* 1979, 17, 457–78 (Eng). A review with 164 refs.

92: 87642g **Therapeutic applications of vitamin D analogs.** Reeve, J. (Northwick Park Hosp., MRC Clin. Res. Cent., Harrow, Engl. HA1 3UJ). *Br. Med. J.* 1979, 2(6195), 888–90 (Eng). A review with 41 refs. on the therapeutic applications of *vitamin D* [1406-16-2], *dihydrotachysterol* [67-96-9], 1,25-dihydroxy- [32511-63-0], 25-hydroxy- [19356-17-3], and *1α-hydroxycholecalciferol* [41294-56-8].

92: 87643h **Pharmacokinetics of amphotericin B and flucytosine.** Polak, Annemarie (Pharm. Res. Div., F. Hoffman-La Roche and Co. Ltd., Basel, Switz.). *Postgrad. Med. J.* 1979, 55(647), 667–70 (Eng). A review with 14 refs. of the pharmacokinetics



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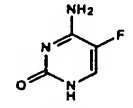
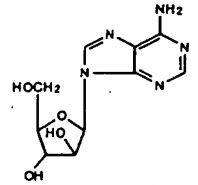


II

of i.v. *amphotericin B* (I) [1397-89-3] and oral *flucytosine* (II) [2022-85-7] and their effect when used clin. alone or in combination.

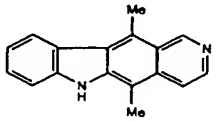
92: 87644j **9-β-D-Arabinofuranosyladenine (AraA).** Cass, Carol E. (Cancer Res. Lab., Edmonton, AB Can. T6G 2H7). *Antibiotics (N. Y.)* 1979, 5(2), 85–109 (Eng). A review with



I

>125 refs. of the biochem. and metab. of *araA* (I) [5536-17-4] and its derivs.

92: 87645k **Ellipticine.** Kohn, Kurt W.; Ross, Warren E.; Glaubiger, Daniel (Natl. Cancer Inst., NIH, Bethesda, MD 20205 USA). *Antibiotics (N. Y.)* 1979, 5(2), 195–213 (Eng).



I

A review with 50 refs. of the pharmacol. of *ellipticine* (I) [519-23-3].

92: 87646m **Parameters and methods in quantitative structure-activity relationships.** Osman, Roman; Weinstein, Harel; Green, Jack Peter (Mount Sinai Sch. Med., City Univ. New York, New York, NY 10029 USA). *ACS Symp. Ser.* 1979, 112(Comput.-Assisted Drug Des.), 21–77 (Eng). A review and discussion with 232 refs.

92: 87647n **Molecular mechanics and crystal structure analysis in drug design.** Duchamp, David J. (Phys. Anal. Chem. Res., Upjohn Co., Kalamazoo, MI 49001 USA). *ACS Symp. Ser.* 1979, 112(Comput.-Assisted Drug Des.), 79–102 (Eng). A review and discussion with 26 refs.

92: 87648p **Anesthesia in gynecology. Blood transfusion in anesthesia.** Takaori, Masuhiko (Kawasaki Med. Coll., Kawasaki, Japan). *Sanfujinka Chiryo* 1979, 39(4), 400–8 (Japan). A review with 20 refs.

92: 87649q **Lung function studies with the bronchospasmolytic terbutalin.** Kaik, G.; Bonelli, J.; Hitzenberger, G.; Laggner, A.; Magometschnigg, D. (Abt. Klin. Pharmakol., 1st Med. Universitaetsklin., Vienna, Austria). *Acta Med. Austriaca, Suppl.* 1979, 14, 1–39 (Ger). Pub. in *Acta Med. Austriaca* 6(2). A review with 400 refs. on the bronchospasmolytic activity

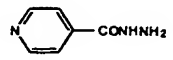
I

of *terbutaline sulfate* (I) [23031-32-5].

92: 87650h **Autonomic nervous system and autonomic drugs in the ophthalmic field. Part II. Autonomic drugs in the ophthalmic field.** Yoo, Hye Young (Coll. Med., Euha Womans Univ., Seoul, S. Korea). *Taehan Ankwa Hakhoe Chapchi* 1979, 20(1), 49–55 (Korean). A review with 21 refs.

B. Namkung

92: 87651j **Clinical pharmacokinetics of isoniazid.** Weber, Wendell W.; Hein, David W. (Med. Sch., Univ. Michigan, Ann Arbor, MI USA). *Clin. Pharmacokinet.* 1979, 4(6), 401–22 (Eng). A review with 163 refs. of the clin. pharmacokinetics of



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isoniazid (I) [54-85-3].

92: 87652k **Development of analgesics.** Koiwa, Shigenori; Amano, Michinosuke (Med. Sch., Keio Univ., Tokyo, Japan). *Ijin Yakujin* 1978, 27(3), 13–14 (Japan). A review with 8 refs. on recent research on analgesics.

92: 87653m **Drug and liver.** Fujisawa, Kiyoshi (Tokyo Jikeikai Med. Coll., Tokyo, Japan). *Ijin Yakujin* 1977, 26(9), 1–4 (Japan). A review with no refs.

92: 87654n **Drug and kidney.** Ebihara, Akio (Jichi Med. Coll., Minami-Kawachi, Japan). *Ijin Yakujin* 1977, 26(9), 5–8 (Japan). A review with 4 refs.

92: 87655p **Enzyme replacement therapy of lysosome storage disease.** Lloyd, John B.; Griffiths, Penelope A. (Dep. Biol. Sci., Univ. Keele, Keele, Engl.). *Front. Biol.* 1979, 48(Lysosomes Appl. Biol. Ther., v6), 517–32 (Eng). A review with ~100 refs.

92: 87656q **Pancreatitis.** Haneshiro, Kiyoshi (Med. Sch., Kinki Univ., Osaka, Japan). *Ijin Yakujin* 1978, 27(1), 7–9 (Japan). A review with 14 refs. on the pharmacol. of pancreatitis.

92: 87657r **Rheumatism.** Higashi, Takeshi (Jieitai Chuo Hosp., Japan). *Ijin Yakujin* 1978, 27(1), 10–12 (Japan). A review with no refs. on the therapy of rheumatism and drug side effects.

92: 87658s **Chemotherapy for physiological shock.** Ishiyama, Satoshi (Med. Sch., Tokyo Univ., Tokyo, Japan). *Ijin Yakujin* 1978, 27(1), 13–18 (Japan). A review with no refs.

92: 87659t **Asthma.** Satake, Tatsuo (Med. Sch., Nagoya Univ., Nagoya, Japan). *Ijin Yakujin* 1978, 27(1), 19–21 (Japan). A review with no refs. on the pharmacol. of asthma.

AN - 1994-028627 [04]
AP - JP19920136731 19920528
PR - JP19920136731 19920528
TI - Marker for early diagnosis of alpha-2u globulin renal disease - for use in SDS-polyacrylamide gel electrophoresis or radioimmunoassay
IW - MARK EARLY DIAGNOSE ALPHA GLOBULIN RENAL DISEASE POLYACRYLAMIDE GEL ELECTROPHORESIS RADIOIMMUNOASSAY
PA - (SUMO) SUMITOMO CHEM CO LTD
PN - JP5333025 A 19931217 DW199404 G01N33/50 003pp
ORD - 1993-12-17
IC - C07K15/06 ; G01N33/50 ; G01N33/53 ; G01N33/68
FS - CPI;EPI
DC - B04 S03
AB - J05333025 Kidney type alpha(2u)-globulin which is useful as marker for the diagnosis of alpha(2u)-globulin renal disease.
- Also claimed is a method for the diagnosis of alpha(2u)-globulin renal disease which uses kidney type alpha(2u)-globulin present in urine.
- When some kinds of chemical substances such as d-limonene or 2,4,4-trimethylpentane are continuously dosed in matured male rat, a renal disease is caused. When alpha(2u)-globulin relaters to the disease, it is called alpha(2u)-globulin renal disease.
- USE/ADVANTAGE - A marker for the early diagnosis of alpha(2u)-globulin renal disease of male rat induced by chemical substance and a method for early stage screening of chemical substance inducing alpha(2u)-globulin renal disease using a marker. The early diagnosis of alpha(2u)-globulin renal disease of male rat can be achieved by e.g., SDS-polyacrylamide gel electrophoresis or radioimmunoassay using antibody without killing rat and chemical substance inducing the disease can be simply screened. (Dwg.0/0)

100: 154351k **Further clues concerning the vectors essential to regulation of hexose transport, as studied in fibroblast cultures from a metabolic mutant.** Kalckar, Herman M.; Ullrey, Donna B. (Dep. Chem., Boston Univ., Boston, MA 02215 USA). *Proc. Natl. Acad. Sci. U. S. A.* 1984, 81(4), 1126–9 (Eng). A close study of the metabolic regulation of hexose transport in a hamster fibroblast mutant, highly defective in the enzyme phosphoglucose isomerase (PGI mutant), reveals the requirement for ≥3 vectors for transport regulation. The downward regulation of the hexose transport system, called the transport curb, requires (*1*) a ligand for the transport system, (*2*) oxidative energy metab., and (*3*) some specific enzymes of glucose 6-phosphate metab. Deprivation of glucose deprives the PGI mutant of UDP-hexose, whereas the glucose-fed mutant contains high levels. The parental strain preserves the UDP-hexose with or without glucose feeding. Cycloheximide added to the mutant shows 2 different types of effects. If added at the onset of glucose starvation, the up-regulation of the transport system was scarcely affected. If cycloheximide was added to the mutant at the onset of glucose refeeding, it prevented the development of the glucose-mediated transport curb. In the mutant, the glucose-mediated curb is not derived from energy metab., but is solely dependent on certain enzymes of glucose 6-phosphate metab. The interference of this curb by cycloheximide evidently requires a reassessment, including that of the role of the UDP-hexose pathway in regulation of the hexose transport system.

100: 154352m **Benzylamine metabolism at low oxygen concentrations. Relative sensitivities of monoamine oxidase, aldehyde dehydrogenase and hippurate synthesis to hypoxia.** Jones, Dean P. (Sch. Med., Emory Univ., Atlanta, GA 30322 USA). *Biochem. Pharmacol.* 1984, 33(3), 413–17 (Eng). The O_2 dependence of the metab. of benzylamine to benzaldehyde, benzoate, and hippurate was studied in isolated rat hepatocytes. The initial oxidn. to benzaldehyde, catalyzed by monoamine oxidase, had an apparent K_m for O_2 of 34 μM in cells and 40 μM in isolated rat liver mitochondria. These values are consistent with the O_2 dependence of bioenergetic changes in these prepns. and indicate that the O_2 dependence of hippurate formation is due to ATP availability for synthesis of benzoyl-CoA. Thus, the 3 metabolic processes involved in benzylamine metab. have markedly different dependences on O_2 and that metab. of benzylamine by monoamine oxidase is O_2 dependent over a physiol. important range.

100: 154353n **Regulation of heme metabolism and cytochrome P 450 levels in primary culture of rat hepatocytes in a defined medium.** Evarts, Ritva P.; Marsden, Elizabeth; Thorgeirsson, Snorri S. (Lab. Carcinog. Metab., Natl. Cancer Inst., Bethesda, MD 20205 USA). *Biochem. Pharmacol.* 1984, 33(4), 565–9 (Eng). Liver cells were prepd. from adult rats and used for the detn. of δ-aminolevulinic acid synthetase (ALAS) activity and cytochrome P 450 (I) concns. at different time intervals in tissue culture in a serum-free synthetic medium. During the 1st 24 h in culture, the level of I 450 decreased to 30–40% of the level in isolated liver cells from untreated animals. The disappearance of I was esp. fast in hepatocytes obtained from female phenobarbital-treated rats where only 40% of the original I was present after 2 h in culture and 80% had disappeared in 2 days. The activity of ALAS increased 3–4-fold when measured 2 h after plating, and it reached the max. level in 19–24 h when its activity was ~8-fold the original activity. In 2–4 days in culture, the activity of ALAS was 4–5-fold above the original level. When the amt. of δ-aminolevulinic acid (ALA) in the medium was increased from 1 to 100 μM, a decrease in ALAS was obtained, but no significant increase in I level was obsd. Addn. of heme to the medium gave a dose-dependent decrease in the activity of ALAS. During the 1st 24 h in culture the increase of ALAS activity apparently was prevented by exogenous heme. This effect may be due to inhibition of the catalytic activity, suppression of the synthesis of the enzyme, or accelerated breakdown of the enzyme by heme.

100: 154354p **Uptake and degradation of iodine-125-labeled rat asialoorosomucoid by the perfused rat liver.** Dennis, Patricia A.; Aronson, Nathan N., Jr. (Program Biochem., Pennsylvania State Univ., University Park, PA 16802 USA). *Biochim. Biophys. Acta* 1984, 798(1), 14–20 (Eng). The uptake and degrdn. of a homologous rat serum asialoglycoprotein, ^{125}I-labeled asialoorosomucoid, and the effects on this metab. by leupeptin, a proteinase inhibitor, were studied in the perfused rat liver. ^{125}I-labeled asialoorosomucoid was rapidly taken up by the liver (half-time = 5.7 min) and acid-sol. degrdn. products began to appear in the circulating perfusate medium after 20–30 min. These products accounted for 60–65% of the initially added radioactivity after 90 min of perfusion. The early events in the galactose-mediated uptake of ^{125}I-labeled asialoorosomucoid were unchanged by the presence of leupeptin. However, the appearance of acid-sol. degrdn. products was greatly reduced when livers had been pretreated with the inhibitor (1.0 mg for 60 min). This effect corresponded with an increase in acid-precipitable material being located within the lysosome-rich fraction from homogenates of leupeptin-treated livers. Leupeptin inhibited degrdn. of ^{125}I-labeled asialoorosomucoid by ~85% relative to control values over 90 min of perfusion. Inhibition of asialoorosomucoid degrdn. was also demonstrated in vitro. Leupeptin (1.0 mM) reduced hydrolysis of this glycoprotein substrate by >50% during a 24-h incubation with isolated lysosomal enzymes. The thiol proteinases, cathepsin B, H, and L, which are known to be inhibited by leupeptin, are apparently involved in initiating digestion of rat ^{125}I-labeled asialoorosomucoid within liver lysosomes. As a result of inhibition by leupeptin both in the perfused liver and in vitro, very limited changes occurred in the native mol. wt. of the starting glycoprotein.

100: 154355q **Intrahepatic assembly of very-low-density lipoproteins. Phosphorylation of small-molecular-weight apolipoprotein B.** Davis, Roger A.; Clinton, Gail M.; Borchardt, Roy A.; Malone-McNeal, Monica; Tan, Tina; Lattier, Gerri R. (Med. Sch., Louisiana State Univ., New Orleans, LA 70112 USA). *J. Biol. Chem.* 1984, 259(6), 3383–6 (Eng). The possibility that apolipoprotein B (apo-B) is phosphorylated was examd. using cultured rat hepatocytes. Rabbit antiserum prepd. against rat apo-B reacted specifically with both large- and small-mol.-wt. apo-B (by electroblotting assay and by immunopptn. of [^{35}S]methionine-labeled proteins synthesized and secreted by hepatocytes). Following a 4-h incubation with [^{32}P]orthophosphate, immunopptn., and SDS electrophoresis, an autoradiog. band corresponding to small-mol.-wt. apo-B was obtained from cells and medium. Compared to the relative abundance of ^{32}P which was assocd. with secreted small-mol.-wt. apo-B, there was little (if any) detected in large-mol.-wt. apo-B. Addn. of excess unlabeled apo-B (obtained from rat serum) totally competed with the specific antiserum for this radioactive protein, indicating it was antigenically related to apo-B. Moreover, isolation of the ^{32}P-labeled apo-B electrophoretic band, followed by acid hydrolysis and phosphoamino acid anal., showed that ≥20% of the ^{32}P originally assocd. with small-mol.-wt. apo-B was in the form of phosphoserine. Control expts. ruled out the possible contamination of apo-B with phospholipid as well as the possibility that the phosphoserine produced by acid hydrolysis could have been derived from phosphatidylserine. To examine the relevance of these data in the in vivo state, rats were injected with [^{32}P]orthophosphate. Immunopptn. of their livers followed by autoradiog. anal. showed the presence of ^{32}P in small-mol.-wt. apo-B. Thus, small-mol.-wt. apo-B is synthesized as a phosphoserine-contg. protein.

100: 154356r **Wide distribution of pH-dependent service of transport system ASC for both anionic and zwitterionic amino acids.** Vadgama, Jaydutt V.; Christensen, Halvor N. (Dep. Biol. Chem., Univ. Michigan, Ann Arbor, MI 48109 USA). *J. Biol. Chem.* 1984, 259(6), 3648–52 (Eng). Criteria have been set up for recognizing the trait of interconvertibility of transport System ASC, whereby it operates in a deprotonated form to mediate the transport of zwitterionic amino acids and in a protonated form to transport anionic amino acids. This trait has been detected by each criterion applied, in all the tested occurrences of System ASC, as follows: the Ehrlich ascites tumor cell in suspension; a cultured variant thereof in monolayer; the CHO-K1 cell in monolayer; the pigeon red blood cell in suspension; and the human red blood cell in suspension. Evidently, this trait is a general feature of System ASC which may be used provisionally in defining the system.

100: 154357s **Monoclonal antibodies to α_{2u}-globulin and immunocytofluorometric analysis of α_{2u}-globulin-synthesizing hepatocytes during androgenic induction and aging.** Motwani, Nalini M.; Caron, Diane; Demyan, William F.; Chatterjee, Bandana; Hunter, Susan; Poulik, Miroslav D.; Roy, Arun K. (Dep. Biol. Sci., Oakland Univ., Rochester, NY 48063 USA). *J. Biol. Chem.* 1984, 259(6), 3653–7 (Eng). Stable hybridomas generated by fusion of spleen cells from hyperimmunized mice and mouse myeloma cells were cloned to prep. monoclonal antibodies to α_{2u}-globulin, an androgen-dependent urinary protein of hepatic origin. One of these monoclonal antibodies was used as a probe for immunocytofluorometric anal. of α_{2u}-globulin-producing hepatocytes during androgenic induction and aging through fluorescence-activated cell sorting (FACS). FACS patterns of hepatocytes from mature male rats that produce high levels of α_{2u}-globulin showed 2 distinct peaks, arbitrarily designated as peak I (weakly fluorescent) and peak II (brightly fluorescent). In the mature male rat, peak II represented ~40% of the total hepatocytes, and the fluorescence intensity of this subpopulation decreased in direct correspondence with the gradual decline of α_{2u}-globulin synthesis during aging. Similarly the androgenic induction of this protein in ovariectomized female rats was assocd. with an increase in the fluorescence intensity of the hepatocyte subpopulation under peak II rather than an increase in the relative no. of these cells. Thus, the androgen-dependent synthesis of α_{2u}-globulin and its alteration during aging are confined to a specific subpopulation of hepatocytes within the liver.

100: 154358t **Heavy isotope-labeling study of the metabolism of monomeric and tetrameric acetylcholinesterase forms in the murine neuronal-like T 28 hybrid cell line.** Lazar, Monique; Salmeron, Eva; Vigny, Marc; Massoulie, Jean (Lab. Biochim. Cell., Coll. France, 75005 Paris, Fr.). *J. Biol. Chem.* 1984, 259(6), 3703–13 (Eng). Heavy isotope labeling was used to study the metabolic turnover of acetycholinesterase (I) forms in the neuroblastoma-derived T 28 hybrid cells in their differentiated state. These cells contain mostly G_1 and G_4 forms, together with a small proportion of G_2, and secrete all these forms into the culture medium. The cells maintained const. and equal levels of I, with the same proportions of mol. forms, in a medium contg. heavy isotope-labeled amino acids and in a control light medium of similar compn. In addn., they secreted I at the same rate in both media. After transfer of the cells into the heavy medium, heavy isotope-labeled I mols. progressively replace preexisting light mols. Heavy and light components of I were analyzed for each of the 2 major G_1 and G_4 forms, by reconstructing the pattern obtained in sucrose gradient differential sedimentation, using combinations of weighted elementary distributions. Heavy mols. were detected in cellular exts. after ~30 min for G_1 and 3 h for G_4. Both heavy forms also appeared in the medium after a log of ~3 h. The cellular complement of G_1 was renewed much faster than that of G_4, the levels of the light forms being reduced to 50% of the original level after 3.5 and 40 h, resp. Each of these forms appeared to consist of several metabolic pools, and simplified models were presented which describe their possible relationships.

CHEMICAL ABSTRACTS®

V 1. 100 MAY 7, 1984 No. 19

1—PHARMACOLOGY

C. PAUL BIANCHI

This section includes the biochemical, physiological, and toxic effects of drugs or potential drugs, their metabolism, analysis in biological systems, and structure–activity relations. Drug formulations are included in Section 63; analysis of drug formulations appears in Section 64; the pharmacology of hormones and agents affecting reproduction, e.g., contraceptives, in Section 2; radiopharmaceuticals, in Section 8; effects of antibiotics, bactericides, etc., on microorganisms in vitro are placed in Section 10; studies emphasizing the synthesis of drugs are included in the appropriate synthetic organic or inorganic section; drugs used only as investigative or diagnostic tools appear in the section appropriate to the organism or process under investigation.

100: 150466d **Nitrosation of drugs.** Eisenbrand, G. (Fachbereich Chem., Univ. Kaiserslautern, 6750 Kaiserslautern, Fed. Rep. Ger.). *Nitrosamin-Probl., Ber. Abschlusskolloq.* 1982 (Pub. 1983), 213–21 (Ger). Edited by Preussmann, Rudolf. Verlag Chem.: Weinheim, Fed. Rep. Ger. A review without refs.

100: 150467e **Drug design by the method of receptor fit.** Goodford, Peter J. (Lab. Mol. Biophys., Oxford, UK). *J. Med. Chem.* 1984, 27(5), 557–64 (Eng). A review with 58 refs.

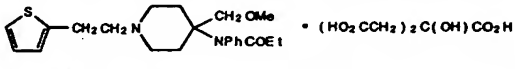
100: 150468f **The free-living nematode Caenorhabditis elegans as a rapid screen for compounds to retard aging.** Zuckerman, Bert M. (Lab. Exp. Biol., Univ. Massachusetts, East Wareham, MA 02538 USA). *Mod. Aging Res.* 1983, 3B(Intervent. Aging Process, Pt. B), 275–85 (Eng). A review with 27 refs.

100: 150469g **Neonatal 'pulmonary vasodilator' drugs. Current status.** Drummond, Willa H.; Lock, James E. (Coll. Med., Univ. Florida, Gainesville, FL USA). *Dev. Pharmacol. Ther.* 1984, 7(1), 1–20 (Eng). A review with 117 refs., on the vascular reactivity of the neonatal pulmonary bed, and on the pharmacol. of neonatal pulmonary vasodilators.

100: 150470a **The steroidal actions of digitalis.** Le Winn, Edward B. (Albert Einstein Med. Cent., Philadelphia, PA 18972 USA). *Perspect. Biol. Med.* 1984, 27(2), 183–99 (Eng). A review with 66 refs.

100: 150471b **Clinical pharmacology of metronidazole.** Ni, Zhong (Tianjin Hebei Pharm. Plant, Tianjin, Peop. Rep. China). *Jiangsu Yiyao* 1983, 9(11), 612–14 (Ch). A review with no refs. on the clin. pharmacol. of *metronidazole* **[443-48-1]**.

100: 150472c **Sufentanil citrate: a new opioid analgesic for use in anesthesia.** Rosow, Carl E. (Dep. Anesth., Massachusetts Gen. Hosp., Boston, MA 02114 USA). *Pharmacotherapy (Carlisle, Mass.)* 1984, 4(1), 11–19 (Eng). A review with 15 refs. on the



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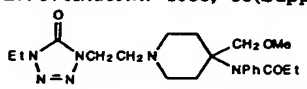
pharmacol. of *sufentanil citrate* (I) **[60561-17-3]** in relation to its use as an analgesic in anesthesia.

100: 150473d **The pharmacokinetics of alfentanil in man.** Hull, C. J. (Dep. Anaesth., Univ. Newcastle upon Tyne, Newcastle upon Tyne, UK). *Br. J. Anaesth.* 1983, 55(Suppl. 2), 157–64 (Eng).



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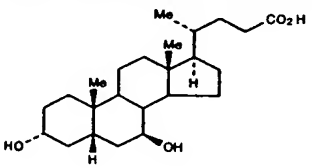
A review with 27 refs. of the pharmacokinetics of *alfentanil* (I) **[71195-58-9]** in man.

100: 150474e **Ursodeoxycholic acid. A review of its pharmacological properties and therapeutic efficacy.** Ward, A.; Brogden, R. N.; Heel, R. C.; Speight, T. M.; Avery, G. S. (ADIS Drug Inf. Serv., Auckland, N. Z.). *Drugs* 1984, 27(2), 95–131 (Eng). A review with ~150 refs. on the pharmacol. of *ursodeoxycholic acid* (I) **[128-13-2]** in relation to treatment of gallstones.



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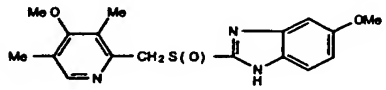
100: 150475f **The role of α-adrenoceptors in the regulation of blood pressure and in the mediation of the antihypertensive effects of drugs.** Van Zwieten, P. A.; Timmermans, P. B. M. W. M. (Div. Pharmacother., Univ. Amsterdam, 1018 TV Amsterdam, Neth.). *Cent. Blood Pressure Regul., Clonidine Workshop* 1982 (Pub. 1983), 7–21 (Eng). Edited by Hayduk, K.; Bock, K. D. Steinkopff: Darmstadt, Fed. Rep. Ger. A review and discussion with 15 refs.

100: 150476g **The psychotropic effects of clonidine.** Jennewein, H. M.; Stockhaus, K.; Lehr, E. (Abt. Pharmakol., Boehringer Ingelheim K.-G., 6507 Ingelheim, Fed. Rep. Ger.). *Cent. Blood Pressure Regul., Clonidine Workshop* 1982 (Pub. 1983), 59–73 (Eng). Edited by Hayduk, K.; Bock, K. D. Steinkopff: Darmstadt, Fed. Rep. Ger. A review with 98 refs. of the psychotropic effects of *clonidine* **[4205-90-7]**.

100: 150477h **Pharmacological basis for the therapeutic use of a gastric proton pump inhibitor.** Olbe, L.; Lind, T.; Carlsson, E.; Cederberg, C.; Helander, H.; Wallmark, B.; Larsson, H. (Serv. Chirur., Sahlgren Hosp., S-413 45 Goeteborg, Swed.). *Med. Hyg.* 1984, 42(1549), 274, 277–8 (Fr). A review with 15 refs. In vitro and



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in vivo expts. demonstrating the inhibitory activity of *omeprazole* (I) **[73590-58-6]** on gastric acid secretion are summarized.

100: 150478j **Surrogate models for antimalarials.** Chou, S. C.; Conklin, K. A.; Levy, M. R.; Warhurst, D. C. (Sch. Med., Univ. Hawaii, Honolulu, HI 96822 USA). *Handb. Exp. Pharmacol.* 1984, 68(Antimalarial Drugs, Part 1), 281–329 (Eng). A review with ~175 refs. on the effects of *chloroquine* **[54-05-7]** and related agents on the cellular uptake and fate of hormones and other ligands, and on the release and uptake of lysosomal enzymes; the effects of protease inhibitors or parasite proteases and on the ability of the parasite to synthesize macromols. is also discussed.

100: 150479k **Neuropharmacological research on nerve cell lines in culture. A way to the limitation of animal experiments.** Herken, Hans (Pharmakol. Inst., Freie. Univ. Berlin, D-1000 Berlin, 33 Fed. Rep. Ger.). *Funkt. Biol. Med.* 1983, 2(3), 125–36 (Ger). A review with 55 refs. of research done by the author and others on using neuronal cell cultures as a substitute for animal expts. in neuropharmacol.

100: 150480d **Adamantanamines - neurobiological studies on the clinical effects of polycyclic compounds with a diamond-like structure.** Wesemann, Wolfgang (Physiol.-Chem. Inst. II, Philipps-Univ., D-3550 Marburg, Fed. Rep. Ger.). *Funkt. Biol. Med.* 1983, 2(3), 137–45 (Ger). A review of 56 refs. of the pharmacol. of adamantane derivs. and analogs. Structure-activity relations are discussed.

100: 150481e **Synergism of physiological, pathological and therapeutic effects.** Poech, Gerald (Inst. Pharmakodyn. Toxikol., Karl-Franzens-Univ., A-8010 Graz, Austria). *Funkt. Biol. Med.* 1983, 2(2), 102–10 (Ger). A review with 42 refs. of synergistic interactions of endogenous compds. and processes among themselves and with drugs, in both physiol. normal and pathol. circumstances.

100: 150482f **Gas chromatography-mass spectrometry for identification of valproic acid metabolites in human serum and urine.** Matsumoto, Isamu (Inst. Hum. Genet., Kanazawa Med. Univ., Uchinada, Japan 920-02). *GC-MS News* 1984, 12(1), 12–13 (Japan). A review with 5 refs.

100: 150483g **Diabetes and drugs.** Molinatti, Gian Michele; Barbero, Pier Luigi; Porta, Massimo (Clin. Med. II, Univ. Torino, Turin, Italy). *Diabete Second., [Atti Conv.]* 1983, 87–101 (Ital). Edited by Greco, A. V.; Chirlanda, G.; Altomonte, L. Field Educ. Italia Acta Medica: Rome, Italy. A review, with 32 refs., of the possible diabetogenic side effects of a no. of drugs and hormones.

100: 150484h **Analysis of the mode of action of antiinflammatory drugs with reference to prostaglandins.** Tsurufuji, Susumu (Fac. Pharm. Sci., Tohoku Univ., Sendai, Japan). *Int. Congr. Ser. - Excerpta Med.* 1983, 623(Perspect. Prostaglandin Res.), 277–82 (Eng). A review with 14 refs.

100: 150485j **Substituted benzimidazoles—a new dimension in ulcer therapy?** Fimmel, C. J.; Blum, A. L. (Med. Klin., Stadtsp. Triemli, CH-8063 Zurich, Switz.). *Wien. Klin. Wochenschr.* 1984, 96(4), 149–53 (Ger). A review with 23 refs.